

MODULE 6

PHARMACISTS

WHO IMPLEMENTATION TOOL FOR PRE-EXPOSURE PROPHYLAXIS (PrEP) OF HIV INFECTION

JULY 2017



WHO/HIV/2017.27

© **World Health Organization 2017**

Some rights reserved. This work is available under the Creative Commons Attribution-NonCommercial-ShareAlike 3.0 IGO licence (CC BY-NC-SA 3.0 IGO; <https://creativecommons.org/licenses/by-nc-sa/3.0/igo>).

Under the terms of this licence, you may copy, redistribute and adapt the work for non-commercial purposes, provided the work is appropriately cited, as indicated below. In any use of this work, there should be no suggestion that WHO endorses any specific organization, products or services. The use of the WHO logo is not permitted. If you adapt the work, then you must license your work under the same or equivalent Creative Commons licence. If you create a translation of this work, you should add the following disclaimer along with the suggested citation: "This translation was not created by the World Health Organization (WHO). WHO is not responsible for the content or accuracy of this translation. The original English edition shall be the binding and authentic edition".

Any mediation relating to disputes arising under the licence shall be conducted in accordance with the mediation rules of the World Intellectual Property Organization.

Suggested citation. WHO Implementation tool for pre-exposure prophylaxis (PrEP) of HIV infection. Module 6: Pharmacists. Geneva: World Health Organization; 2017. Licence: CC BY-NC-SA 3.0 IGO.

Cataloguing-in-Publication (CIP) data. CIP data are available at <http://apps.who.int/iris>.

Sales, rights and licensing. To purchase WHO publications, see <http://apps.who.int/bookorders>. To submit requests for commercial use and queries on rights and licensing, see <http://www.who.int/about/licensing>.

Third-party materials. If you wish to reuse material from this work that is attributed to a third party, such as tables, figures or images, it is your responsibility to determine whether permission is needed for that reuse and to obtain permission from the copyright holder. The risk of claims resulting from infringement of any third-party-owned component in the work rests solely with the user.

General disclaimers. The designations employed and the presentation of the material in this publication do not imply the expression of any opinion whatsoever on the part of WHO concerning the legal status of any country, territory, city or area or of its authorities, or concerning the delimitation of its frontiers or boundaries. Dotted and dashed lines on maps represent approximate border lines for which there may not yet be full agreement.

The mention of specific companies or of certain manufacturers' products does not imply that they are endorsed or recommended by WHO in preference to others of a similar nature that are not mentioned. Errors and omissions excepted, the names of proprietary products are distinguished by initial capital letters.

All reasonable precautions have been taken by WHO to verify the information contained in this publication. However, the published material is being distributed without warranty of any kind, either expressed or implied. The responsibility for the interpretation and use of the material lies with the reader. In no event shall WHO be liable for damages arising from its use.

Layout by L'IV Com Sàrl, Villars-sous-Yens, Switzerland.

Cover Photos: © JohnRaeNYC

Contents

INTRODUCTION	2
THE PHARMACISTS MODULE	4
Possible roles of pharmacists in PrEP services	4
Nomenclature of antiretroviral drugs for PrEP	5
Food and oral absorption of PrEP medicines	5
Drug–drug interactions	5
Medicine handling and storage conditions	6
Recommendations for storage at home	6
Monitoring effective PrEP use	6
Medicine supply	6
Advice for PrEP users	6
REFERENCES	9

Introduction

Following the WHO recommendation in September 2015 that “oral pre-exposure prophylaxis (PrEP) should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination HIV prevention approaches”, partners in countries expressed the need for practical advice on how to consider the introduction of PrEP and start implementation. In response, WHO has developed this series of modules to support the implementation of PrEP among a range of populations in different settings.

Although there is growing acknowledgement of PrEP’s potential as an additional HIV prevention option and countries are beginning to consider how PrEP might be most effectively implemented, there has been limited experience with providing PrEP outside research and demonstration projects in low- and middle-income countries. Consequently, there is often uncertainty around many implementation issues. The modules in this tool provide initial suggestions for the introduction and implementation of PrEP based on currently available evidence and experience. However, it is recognized that this evidence may evolve following wider PrEP use; therefore, it is likely that this tool will require regular updating.

PrEP should not replace or compete with effective and well-established HIV prevention interventions, such as comprehensive condom programming for sex workers and men who have sex with men and harm reduction for people who inject drugs. Many people who could benefit most from PrEP belong to key population groups that may face legal and social barriers to accessing health services. This needs to be considered when developing PrEP services. Although the public health approach underpins the WHO guidance on PrEP, the decision to use PrEP should always be made by the individual concerned.

Target audience and scope of tool

This PrEP tool contains modules for a range of stakeholders to support them in the consideration, planning, introduction and implementation of oral PrEP. The modules can be used on their own or in combination. In addition, there is a module for individuals interested in or already taking PrEP. (See Summary of modules below.)

This tool is the product of collaboration between many experts, community organizations and networks, implementers, researchers and partners from all regions. The information presented is aligned with WHO’s 2016 consolidated guidelines on the use of antiretroviral drugs for HIV treatment and prevention.

All modules make reference to the evidence-based 2015 WHO recommendation on PrEP. They do not make any new recommendations on PrEP, focusing instead on suggested implementation approaches.

Guiding principles

It is important to adopt a public health, human rights and people-centred approach when offering PrEP to those at substantial risk of HIV. Similar to other HIV prevention and treatment interventions, a human rights-based approach gives priority to issues concerning universal health coverage, gender equality and health-related rights including accessibility, availability, acceptability and quality of PrEP services.

SUMMARY OF MODULES



Module 1: Clinical. This module is for clinicians, including physicians, nurses and clinical officers. It gives an overview of how to provide PrEP safely and effectively, including: screening for substantial risk of HIV; performing appropriate testing before initiating someone on PrEP and while the person is taking PrEP; and how to follow up PrEP users and offer counselling on issues such as adherence.



Module 2: Community educators and advocates. For PrEP services to reach populations in an effective and acceptable way, community educators and advocates are needed to increase awareness about PrEP in their communities. This module provides up-to-date information on PrEP that should be considered in community-led activities that aim to increase knowledge about PrEP and generate demand and access.



Module 3: Counsellors. This module is for staff who counsel people as they consider PrEP or start taking PrEP and support them in addressing issues around coping with side-effects and adherence strategies. Those who counsel PrEP users may be lay, peer or professional counsellors and healthcare workers, including nurses, clinical officers and doctors.



Module 4: Leaders. This module aims to inform and update leaders and decision-makers about PrEP. It provides information on the benefits and limitations of PrEP so that they can consider how PrEP could be most effectively implemented in their own settings. It also contains a series of frequently asked questions about PrEP, with related answers.



Module 5: Monitoring and evaluation. This module is for people responsible for monitoring PrEP programmes at the national and site levels. It provides information on how to monitor PrEP for safety and effectiveness, suggesting core and additional indicators for site-level, national and global reporting.



Module 6: Pharmacists. This module is for pharmacists and people working in pharmacies under a pharmacist's supervision. It provides information on the medicines used in PrEP, including the optimal storage conditions. It also gives suggestions for how pharmacists and pharmacy staff can monitor PrEP adherence and support PrEP users to take their medication regularly.



Module 7: Regulatory officials. This module is for national authorities in charge of authorizing the manufacturing, importation, marketing and/or control of antiretroviral medicines used for HIV prevention. It provides information on the safety and efficacy of PrEP medicines.



Module 8: Site planning. This module is for people involved in organizing PrEP services at specific sites. It outlines the steps to be taken in planning a PrEP service and gives suggestions for personnel, infrastructure and commodities that could be considered when implementing PrEP.



Module 9: Strategic planning. As WHO recommends offering PrEP to people at substantial HIV risk, this module offers public health guidance for policy-makers on how to prioritize services, in order to reach those who could benefit most from PrEP, and in which settings PrEP services could be most cost-effective.



Module 10: Testing providers. This module is for people who are responsible for providing testing services at PrEP sites and associated laboratories. It offers guidance in selecting relevant testing services, including appropriate screening of individuals before PrEP is initiated and monitoring while they are taking PrEP. Information is provided on testing for HIV, creatinine, hepatitis B and C virus, pregnancy and sexually transmitted infections.



Module 11: PrEP users. This module provides information for people who are interested in taking PrEP to reduce their risk of acquiring HIV and people who are already taking PrEP – to support them in their choice and use of PrEP. This module gives ideas for countries and organizations implementing PrEP to help them develop their own tools.

ANNEXES

Review of evidence. A wide range of evidence including the following two systematic reviews informed the 2015 WHO recommendation on PrEP for people at substantial risk of HIV infection: (i) Fonner VA et al. *Oral tenofovir-based HIV pre-exposure prophylaxis (PrEP) for all populations: a systematic review and meta-analysis of effectiveness, safety, behavioural and reproductive health outcomes*; (ii) Koechlin FM et al. *Values and preferences on the use of oral pre-exposure prophylaxis (PrEP) for HIV prevention among multiple populations: a systematic review of the literature*.

Annotated Internet resources. This list highlights some of the web-based resources on PrEP currently available together with the stakeholder groups they are catering to. WHO will continue to provide updates on new resources.

The pharmacists module

Pharmacists and pharmacy workers can play a key role in the provision and monitoring of PrEP.

The World Health Organization (WHO) recommends that medicines containing tenofovir disoproxil fumarate (TDF) be made available as PrEP to prevent HIV infection for people at substantial HIV risk (see box below) (1). Pharmacists and people who work in pharmacies under a pharmacist's supervision can play a key role in the provision and monitoring of PrEP. Pharmacists are often among the healthcare workers most accessible to the public. When dispensing and supplying

PrEP medicines, they have the responsibility to explain the effective and safe use of these medicines to PrEP users. Their key responsibilities also include maintaining optimal storage conditions, such as temperature and humidity control. Further, drugs for HIV treatment and prevention are valuable and require controlled use. Pharmacies have to maintain adequate security against theft, diversion and other unauthorized access.

WHO Recommendation for PrEP

The World Health Organization recommends that PrEP containing TDF should be offered as an additional prevention choice for people at substantial risk of HIV infection as part of combination prevention approaches (*strong recommendation; high-quality evidence*).

Possible roles of pharmacists in PrEP services

Pharmacists ensure that the correct medicine is dispensed at the correct dose to the correct person. They may repackage medicines, in accordance with local regulations, to make them more convenient for PrEP users and to support adherence. Pharmacists and their staff may have multiple roles in providing PrEP, including:

- managing the supply chain and drug procurement
- ensuring accurate dispensing of prescriptions of PrEP medicines in accordance with local regulations
- providing information about PrEP, including counselling to support adherence
- offering advice on possible side-effects and their management
- providing information on the potential for drug–drug interactions
- reassuring that there are no food restrictions when taking PrEP
- explaining that it is safe to take PrEP and drink alcohol
- monitoring adherence of PrEP users when returning for prescription refills.

There are emerging models of PrEP services, and the role of pharmacists is understood as a key element in service delivery, including in the context of community pharmacy settings (2).

People who work in pharmacies may be interested in other modules in this document, e.g. medicines regulators, strategic planning, site planning, clinical and counsellors. Information found in those modules is not repeated here.

Nomenclature of antiretroviral drugs for PrEP

The following table lists the antiretroviral drugs for PrEP (3).

GENERIC NAME & ABBREVIATION	DOSAGE
Tenofovir disoproxil fumarate (TDF) / Emtricitabine (FTC)	Each tablet contains 300 mg of TDF and 200 mg of FTC.
Tenofovir disoproxil fumarate (TDF) / Lamivudine (3TC) ¹	Each tablet contains 300 mg of TDF and 300 mg of 3TC.
Tenofovir disoproxil fumarate (TDF)	Each tablet contains 300 mg (TDF – equivalent to 245 mg tenofovir disoproxil).

Food and oral absorption of PrEP medicines

There are no food or alcohol restrictions when taking PrEP medicines.

People often ask whether they should take medicines with food or on an empty stomach. TDF and emtricitabine (FTC) can be taken with or without food. It is important for pharmacists to inform people taking PrEP about this in order to reassure and support them in taking these medicines when and how it suits them best.

Drug–drug interactions

Medicines used for PrEP and PEP. Lamivudine (3TC) and FTC should not be used together because they are very similar compounds and no additional benefit is expected if they are used at the same time.

Hormonal contraception and sex hormones. TDF, FTC and 3TC do not have any known interactions with contraceptive hormones (4), hormones used for feminization by transgender women or hormones used for masculinization by transgender men.

Other medicines. TDF, FTC and 3TC do not have interactions with most commonly used medicines and can be safely taken at the same time as antidepressants, tuberculosis or malaria medicines. However, TDF is closely related to adefovir, a medicine used to treat hepatitis B virus infections; therefore, TDF and adefovir should not be used together.

Detailed drug–drug interactions can be investigated by using the database maintained by the University of Liverpool at <http://www.hiv-druginteractions.org/checker##table-view-wrap> or the database provided by the University of California, San Francisco at <http://hivinsite.ucsf.edu/interactions>.

Alcohol and recreational drugs. There are no known interactions between PrEP medicines and alcohol or recreational drugs. However, if a PrEP user thinks that his or her use of alcohol, or other substances, is interfering with taking PrEP regularly, the pharmacist could suggest that the person talk to a nurse or doctor and/or contact appropriate local services and support groups.

¹ All three medicines, including the two fixed-dose combinations, are included in the WHO Model List of Essential Medicines (March 2017). TDF/3TC could be an alternative option if TDF/FTC is not available. Although 3TC is equivalent to FTC for HIV treatment, the use of 3TC for PrEP has not been studied in clinical trials except in one Phase I study. Information from clinical services that utilize TDF/3TC PrEP would be helpful. There is limited evidence of the efficacy of TDF alone among men who have sex with men.

Medicine handling and storage conditions

TDF, TDF/FTC and TDF/3TC come with labels from the providers of these generic agents recommending storage at ambient temperatures of 15–30 °C (59–86 °F). All three medicines are available in unit-of-use bottles of 30 tablets with a child-resistant closure and containing a desiccant (silica gel canister or sachet). Pharmacists should keep the container bottles tightly shut and dispense the medicines only in their original containers. If the seal over the bottle opening is broken or missing, the bottle should not be used.

Recommendations for storage at home

Pharmacists and pharmacy workers can encourage PrEP users to:

- keep their PrEP medicine in its original container, together with the desiccant. Users may choose to transfer a seven-day supply to a pill box for travelling or to help them to remember to take the medication daily.
- store the tablets at 15–30 °C (59–86 °F). PrEP users should be advised not to keep their PrEP medication in places that can become very hot (such as a car) or cold (such as a refrigerator).
- keep PrEP medicines out of direct sunlight and protected from moisture.
- keep tablets out of children's reach.

Monitoring effective PrEP use

The effectiveness of PrEP in HIV prevention depends on PrEP users taking their medication daily (5). Pharmacists can play a role in supporting PrEP users to take their medication regularly. It is important to be open and non-judgemental when asking about PrEP use; if users think the pharmacist will be critical of them, they may over-report PrEP consumption and hide problems with adherence or missed tablets.

Monitoring pharmacy refills can help assess whether a PrEP user has been taking the medication regularly.

Monitoring pharmacy refills can be a helpful way to assess whether a PrEP user has been taking the PrEP medicine regularly. A formal way to estimate the consistency of pharmacy refills is to calculate the medication possession ratio (6), that is, the number of tablets dispensed divided by the number of days between refills.

Medicine supply

The optimal number of tablets that should be dispensed at one time has not yet been determined. It will likely vary by setting and population. PrEP discontinuation rates are often highest in the first four weeks (7); therefore, some clinics may prescribe a one-month supply at the first visit and then a three- or four-month supply at subsequent visits. If clinic visits are planned for every three months, for example, sufficient medicine for four months might be provided. The extra month's supply is important in case the next visit is delayed for any reason, and it may help users to avoid rationing tablets as their next clinic visit approaches. Providing an extra month's supply of medicine, if available, at the first clinic visit ensures an adequate supply for daily dosing until the next visit. Clients who have some medicine supply in reserve tend to show better adherence (6).

Advice for PrEP users

When offering advice to users, the simplicity of taking PrEP – just one tablet each day – can be emphasized. In general, PrEP is easy to use: it can be taken with or without food and does not interact with alcohol. PrEP can be taken at any time of day. PrEP provides high levels of protection in people who take it regularly. When people start PrEP, time is needed to build up protective levels in the blood and other tissues. Therefore, additional HIV prevention should be taken for the first seven days of PrEP use.

The following key points can be highlighted during an interaction with a PrEP user:

- Take one tablet each day. It may be easiest to remember if you take the tablet at the same time each day.
- PrEP is highly effective in preventing HIV infection, but it does not protect against other sexually transmitted infections or prevent pregnancy. [Advice about condoms and contraception can be shared where appropriate.]

- PrEP provides high levels of protection in people who take PrEP medicines regularly. As time is needed to build up protective levels of the medicine in the blood and other tissues, additional HIV prevention should be taken for the first seven days of PrEP use.
- If you miss a PrEP dose on a given day and realize this on that same day, you should take your pill as soon as you remember. If you do not remember until the next day, there is no need to take two pills on the same day. Just take one tablet each day as usual.
- In general, keep the tablets in the bottle with the drying agent. However, you can take a few tablets out to carry with you if you wish.
- Try to keep the bottle and tablets away from intense heat or cold and out of the sun and humidity.

Pharmacists can emphasize the simplicity of taking PrEP

Pharmacists can also support and provide tips to PrEP users to help them take their medicine daily (see box).

How a pharmacist or pharmacy worker can help PrEP users to adhere

Ask: "Do you sometimes forget to take your pills? Many people do."

If so, suggest: "You could:

- make pill-taking part of your daily routine by:
 - taking a pill at the same time each day."
 - taking your pill at the same time as another daily activity such as brushing your teeth, having your evening meal or watching your favorite TV programme."
- add a reminder to your phone that alerts you when it is time to take your tablet."
- plan to take a small supply of pills with you when you are staying overnight somewhere else or you are travelling."
- if you plan a long trip, ask your PrEP prescriber to give you a longer prescription to cover the period when you will be away."

If necessary, also suggest: "If you have difficulty taking PrEP regularly:

- tell someone (a trusted friend or family member) that you are taking PrEP and ask them to help you to take it every day."
- talk to another PrEP user about what works for him or her."
- find a PrEP user support group or online PrEP forum."

More detailed information about counselling is available in the module for counsellors.

Questions and answers

The following are some typical questions that PrEP users might address to pharmacy workers, together with suggested answers:

Q: What is the name of the tablet that I will be taking?

A: *[Give the originator or generic name, whichever is prescribed.]*

Q: How should I take PrEP?

A: *Take one tablet each day. PrEP can be taken at any time of day. It does not have to be taken at the same time each day, although this may help you remember. You can take PrEP with or without food. Although it is safe to take PrEP with many other medicines, it will be necessary to check each one specifically. We can help you check if there might be any problems. Please tell me what other medicines you are taking.*

Q: How long should I take PrEP?

A: Until you are no longer at risk of HIV infection.

Q: What are the possible side-effects I could have?

A: Most people have no side-effects. About one in every 10 people may have mild nausea, headache or stomach cramping that can last a few days to a week when they first start PrEP.

Q: Will PrEP affect my weight?

A: Some people taking PrEP think the medicines might cause them to gain or lose weight. Although PrEP medications do not affect a person's weight, there may be other issues associated with using PrEP, such as feeling less anxious, that might lead to an increase in or loss of weight.

Q: How soon does PrEP become effective?

A: A level of protection is gained after two days of taking PrEP medicines; however, full protection comes after seven days.

Q: How does PrEP work?

A: It blocks HIV from spreading in the body.

Q: How can I remember to take a pill every day?

A: Try to choose a time that fits your daily routine, for example taking the tablet after brushing your teeth each morning. Or, if you have a mobile phone, you could set a reminder on the phone at the time you plan to take your tablet.

Q: Do I have to stop drinking alcohol because I am taking PrEP?

A: No, it is safe to take PrEP if you drink alcohol. If, however, you are worried that your use of alcohol or other substances is interfering with your ability to take PrEP regularly, you could talk to a nurse or doctor and/or contact appropriate local services and support groups.

Q: What if I miss a dose?

A: If you miss your tablet on a given day and realize this on that same day, take your pill as soon as you remember. If you do not remember until the next day, there is no need to take two pills on the same day. Just take one tablet each day as usual.

Q: What if I vomit a dose?

A: If the tablet is visibly vomited out, wait for an hour for the vomiting to resolve and take another tablet. If vomiting occurs an hour or more after taking the tablet, or you do not see that the tablet has been vomited out, take your next tablet the next day as usual.

Q: How should I store my PrEP medicine?

A: Try to keep the PrEP medicine in the original container with the desiccant (drying agent). You can transfer a seven-day supply to a pill box for travelling or to help you remember to take your tablet daily. Keep the medicine at room temperature, out of direct sunlight and protect it from moisture. Keep it out of the reach of children.

Q: Since I am using PrEP, can I stop other HIV prevention methods?

A: PrEP is one important method that you can use to protect yourself from HIV infection. No method offers 100% protection. PrEP does not protect against other sexually transmitted infections or pregnancy. While taking your PrEP medicine, you can increase your level of protection by also using:

- condoms
- clean injection equipment if you inject drugs
- contraception to prevent unplanned pregnancy.

Q: Is PrEP safe in pregnancy and during breastfeeding?

A: If you want to get pregnant or are already pregnant, taking PrEP is safe (8). It is a good idea to tell your PrEP provider as soon as possible so you can get the best care. It is safe to take PrEP when you are breastfeeding.

References

1. Consolidated guidelines on the use of antiretroviral drugs for treating and preventing HIV infection. Geneva: World Health Organization; 2016 (http://apps.who.int/iris/bitstream/10665/208825/1/9789241549684_eng.pdf?ua=1).
2. Lehman DA, Baeten JM, McCoy CO, Weis JF, Peterson D, Mbari G, et al. Risk of Drug Resistance Among Persons Acquiring HIV Within a Randomized Clinical Trial of Single-or Dual-Agent Preexposure Prophylaxis. *Journal of Infectious Diseases*. 2015(DOI: 10.1093/infdis/jiu677).
3. WHO Model List of Essential Medicines, 20th List (March 2017). Geneva: World Health Organization; 2017 (http://www.who.int/medicines/publications/essentialmedicines/20th_EML2017.pdf?ua=1).
4. Nanda K, Stuart GS, Robinson J, Gray AL, Tepper NK, Gaffield ME. Drug interactions between hormonal contraceptives and antiretrovirals. *AIDS*. 2017;31(7):917-52.
5. Fonner VA, Dalglish SL, Kennedy CE, Baggaley R, O'Reilly KR, Koechlin FM, et al. Effectiveness and safety of oral HIV preexposure prophylaxis for all populations. *AIDS*. 2016;30(12):1973-83.
6. Amico KR, Marcus JL, McMahan V, Liu A, Koester KA, Goicochea P, et al. Study product adherence measurement in the iPrEx placebo-controlled trial: Concordance with drug detection. *J Acquir Immune Defic Syndr*. 2014.
7. Grant RM, Anderson PL, McMahan V, Liu A, Amico KR, Mehrotra M, et al. Uptake of pre-exposure prophylaxis, sexual practices, and HIV incidence in men and transgender women who have sex with men: a cohort study. *The Lancet Infectious Diseases*. 2014;14(9):820-9.
8. Mofenson LM, Baggaley RC, Mameletzis I. Tenofovir disoproxil fumarate safety for women and their infants during pregnancy and breastfeeding. *AIDS*. 2017;31(2):213-32.



For more information, contact:

World Health Organization
Department of HIV/AIDS
20, avenue Appia
1211 Geneva 27
Switzerland

E-mail: hiv-aids@who.int

www.who.int/hiv